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EXAMINER	
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ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
04/30/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/561,902	SCHULE ET AL.	
	Examiner	Art Unit	
	KELAGINAMANE T. HIRIYANNA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *7-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/06; 02/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Restriction of invention

Applicant's election with traverse of restriction requirement in the reply filed on Feb 14, 2008 is acknowledged. Applicant elects with traverse the invention Group I (Claims 1-6) for further prosecution on merits. Applicant traverses on the grounds that it would not pose an undue burden on the examiner to examine all the claims. However, for the reasons set forth in the office action of dated Jan 15, 2008, the Applicants arguments are not found persuasive and hence the rejection is made final.

Claims 1-6 are pending and presently under examination.

Claims 7-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected claims, there being no allowable generic or linking claim.

Claim Objections

Claims 2-5 are objected to because of the following formalities: While claiming dependence on the subject of previous claim referring to "The" subject of previous claim rather than "A", is proper format. Accordingly, "A method..." in claims 2-5 should read "The method...". Appropriate correction is required.

Claims 1-5 are objected to because of the following formalities: While the primary claim (claim 1) recites in the preamble on line 1-2 "the activity of osteoblasts...." , the step (b) of the claim recites a genus of activity "an activity.....". Similarly the steps in the dependent claims recite more than one activity being promoted in cells. Dependent claim steps meant to modify or limit the steps of the primary claim rather than creating a new step. Thus the preamble and the steps are not commensurate with each other. However, as the Artisan would understand what is being claimed, no rejection is made. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying compounds that promote osteoblast extracellular matrix deposition, comprising contacting an osteoblast with a test compound in vitro; determining Fhl2 protein levels in the cell; comparing such protein level to a control osteoblast that has not been contacted with a test compound; and selecting those compounds that increase Fhl2 protein levels, but not for the breadth of any cell type; the breadth of any activity of the Fhl2 gene or protein; the breadth of compounds that decrease Fhl2 protein levels; the breadth of control cells that are not the same osteoblast cell type as those tested; or the preparation of any compound for therapeutic purposes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of invention as claimed encompasses any compound that promotes "the activity" of an osteoblast derived from any animal, any activity of Fhl2 gene or any activity of Fhl2 protein upon on contact and measuring said activities and selecting a compounds that increases or decreases said activities significantly as compared to a control cell that is not contacted by said compound and thereby promoting the activity of the osteoblast, any compound that increases interaction of Fhl2 with Runx2 protein in an osteoblast and promoting the activity of osteoblast and further encompsses synthesizing any of said compounds and use them in treating any and or all bone diseases.

The specification at best teaches "the activity of osteoblast" is that of promoting deposition of extracellular matrix. It appears from the examples and explanation that (1) increased Fhl2 expression is correlated with Runx2-induced transcriptional activity; and (2) that Fhl2 binds to Runx2 in the cell. Still further, animals not expressing Fhl2 have diminished bone formation.

Applicant does not disclose any compound other than the Fhl2 transgene expression that could promote an increase in expression or activity of Fhl2 in an osteoblast, does not disclose any compound other than said transgene that could cause an increase in levels of Fhl2 protein inside the nucleus of an osteoblast and still further does not disclose any compound that increases Runx2 protein interaction with Fhl2 protein in an osteoblast. Further applicant does not disclose any mechanisms, by which a compound could increase the activities of Fhl2 such that it would increase/decrease the interaction with Runx2 sufficiently (for example by specific mutations in Fhl2) so as to cause an increased/decreased matrix deposition and/or an increase/decrease bone formation and further it is unpredictable to the artisan that both an increase and/or decrease in the expression of Fhl2 would have similar affects on the activity of an osteoblast.

Art at the time of invention art only teaches regarding an increase in Fhl2 activity in an osteoblast is achieved by over expressing an Fhl2 transgene in said osteoblast (Amaar et al., 2002, J. Biol. Chem. 277:12503-12059 and Lai et al., 2002, J. Bone and Mineral Res. Vol.17; supp (1), pp. S129; art of record) and an increase in cell proliferation. An elevation of activities certain enzymes, osteopontin and bone sialoprotein, an upregulation of osteocalcin and bone mineralization along with synergized Cbfa1 (Runx2) and FGF2 activities were also observed in these cells (Lai et al; supra). However, neither the art nor the specification teach regarding how a simple delivery of a compound could be of any therapeutic value for treating any and/or all bone diseases as broadly claimed.

Art clearly teaches several bone disorders that are not caused by or due to a decrease in extra-cellular matrix secretion or the activity of osteoblasts per se (e.g., bone cancer and metastasis, bone diseases/disorders due to nutritional deficiencies, several genetic bone disease etc; for example see Keller et al, 2007, J. Cellular Biochem. 102:1095-1102) and hence one of ordinary skill in the art would not reasonably be able to predict that a compound that affects Fhl2 gene expression or Fhl2 activity in an osteoblast could be of any therapeutic value for treating such bone diseases.

Since the specification fails to disclose any of the broadly claimed compounds, other than an over expression of Fhl2 transgene, could promote the osteoblast activity either by increasing or by decreasing a Fhl2 gene activity including Fhl2 gene expression or by increasing an Fhl2 protein activity or by Fhl2 protein accumulation in a osteoblast nucleus or by increasing or decreasing Fhl2 protein interaction with Runx2 protein in said cell and since. The specification further fails to disclose synthesis of said compounds or their use in treating any and/or all the bone diseases as broadly claimed. The applicant's disclosure thus does not reasonably enable one skilled in the art to practice the invention as claimed without further undue amount of experimentation, which requires the artisan to screen any and/or all compounds and further researching using all possible broadly claimed method steps to identify a compounds that modulate Fhl2 activity or interactions, synthesize the positively identified compounds, determine their therapeutic potential and use them for treating a bone disease. Further the invention is unpredictable as claimed because the applicant and the art only teach regarding promoting an osteoblast activity by increased level of expression Fhl2 activity in the osteoblast and not by decreasing the Fhl2 activity or expression or interactions whereas the scope of the instant claims encompass both increase and decrease in the same for promoting the activity of the osteoblast (as defined). At issue, under the enablement requirement of 35 U.S.C. 1 12, first paragraph is whether, given the Wands-factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See Fields v. Conover, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in

Claims 1-4 are rejected under 35 USC 102 (b) as being anticipated by Amaar et al (2002, J. Biol. Chem. 277:12503-12059).

The above claims are directed to a method of screening compounds that promote the activity of osteoblasts in vitro by modulating the cellular activity of Fhl2 gene or Fhl2 protein.

Regarding the claims 1-4 Amaar teaches over expressing FHL2 gene and protein in bone cells (U2 osteoblasts or osteosarcoma cells) in vitro by contacting FHL2 cDNA (a compound) cloned in retroviral expression vector (p.12054, col.2, paragraph 8 bridging p.1205; p.12059, col.1, paragraphs 3-5 bridging col.2). The cited art thus anticipates the invention as claimed.

Claims 1-5 are rejected under 35 USC 102 (b) as being anticipated by Lai et al (2002, J. Bone and Mineral Res. Vol.17; supp (1), pp. S129; art of record).

The above claims are directed to a method of screening compounds that promote the activity of osteoblasts in vitro by modulating the cellular activity of Fhl2 gene or Fhl2 protein.

Regarding the claims 1-5 Lai teaches over expressing FHL2 gene and protein in osteoblasts (MC3T3-E1) in vitro by contacting FHL2 cDNA (a compound) cloned in a expression vector (Abstract). Lai further teaches Fhl2 expression is up regulated in these cells which further show an cell proliferation, matrix mineralization, osteocalcin up regulation and Runx2 (Cbfa1) up regulation . Lai further teaches that FHL2 may play an important role in bone formation. The cited art thus anticipates the invention as claimed.

Conclusion

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Kelaginamane Hiriyanna Ph.D., whose telephone number is (571) 272-3307. The examiner can normally be reached Monday through Friday from 9 AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach Ph.D., may be reached at (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

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